In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

In the Claims:

1. (Currently Amended) A conjugate comprising:

(a) a polypeptide having the amino acid sequence :

$$[Yn\cdots Y_1]ZX_1X_2X_3S(p)[W_1\cdots Wm]$$

wherein,

m equals 1 or 2;

n is an integer from ~~3~~1 to ~~7~~50, such that said polypeptide consists of 10 to 13 amino acid residues;

S(p) is a phosphorylated serine residue or a phosphorylated threonine residue;

Z is any amino acid residue excepting serine residue or threonine residue; and

X_1, X_2, X_3, Y_1-Yn and W_1-Wm are each independently any amino acid residue; and

(b) at least one hydrophobic moiety being attached to said polypeptide, said at least one hydrophobic moiety comprising a fatty acid,

the conjugate being capable of inhibiting an activity of glycogen synthase kinase-3 (GSK-3), wherein the hydrophobic moiety provides the conjugate with better (i) membrane permeability and/or (ii~~b~~) interaction with the hydrophobic patch of the GSK-3.

2. (Original) The conjugate of claim 1, wherein said at least one hydrophobic moiety is attached to an N-terminus and/or a C-terminus of said polypeptide.

3-6. (Canceled)

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

7. (Currently Amended) The conjugate of claim ~~6~~ 1, wherein said at least one hydrophobic moiety further comprises an~~fatty acid is attached to at least one~~ amino acid residue attached to said fatty acid.

8. (Currently Amended) The conjugate of claim ~~6~~ 1, wherein said fatty acid is selected from the group consisting of myristic acid, lauric acid, palmitic acid, stearic acid, oleic acid, linoleic acid and linolenic acid.

9. (Canceled)

10. (Original) The conjugate of claim 1, wherein Y_3 is any amino acid residue except a glutamic acid residue.

11. (Original) The conjugate of claim 1, wherein Z is an alanine residue.

12-13. (Canceled)

14. (Original) The conjugate of claim 1, having the amino acid sequence set forth in SEQ ID NO:16.

15. (Original) A pharmaceutical composition comprising, as an active ingredient, the conjugate of claim 1, and a pharmaceutically acceptable carrier.

16. (Original) The pharmaceutical composition of claim 15, packaged in a packaging material and identified in print, on or in said packaging material, for use in the treatment of a biological condition associated with GSK-3 activity.

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

17. (Original) The pharmaceutical composition of claim 16, wherein said biological condition is selected from the group consisting of obesity, non-insulin dependent diabetes mellitus, an insulin-dependent condition, an affective disorder, a neurodegenerative disease or disorder and a psychotic disease or disorder.

18-23. (Canceled)

24. (Original) The pharmaceutical composition of claim 15, further comprising at least one additional active ingredient that is capable of altering an activity of GSK-3.

25. (Original) The pharmaceutical composition of claim 24, wherein said additional active ingredient is insulin.

26. (Original) The pharmaceutical composition of claim 24, wherein said additional active ingredient is capable of inhibiting an activity of GSK-3.

27. (Canceled)

28. (Original) The pharmaceutical composition of claim 24, wherein said additional active ingredient is capable of downregulating an expression of GSK-3.

29-45. (Canceled)

46. (Currently Amended) A method of inhibiting an activity of GSK-3, the method comprising contacting cells expressing GSK-3 with an effective amount of a~~the~~ conjugate comprising:

(a) a polypeptide having the amino acid sequence :

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

[Yn···Y_1]Z$X_1X_2X_3$S(p)[W_1···Wm]

wherein,

m equals 1 or 2;

n is an integer from 1 to 50;

S(p) is a phosphorylated serine residue or a phosphorylated threonine residue;

Z is any amino acid residue excepting serine residue or threonine residue; and

X_1, X_2, X_3, Y_1-Yn and W_1-Wm are each independently any amino acid residue; and

(b) at least one hydrophobic moiety being attached to said polypeptide,

the conjugate being capable of inhibiting an activity of glycogen synthase kinase-3 (GSK-3), wherein the hydrophobic moiety provides the conjugate with better (i) membrane permeability and/or (ii) interaction with the hydrophobic patch of the GSK-3 ~~of claim 1~~.

47. (Original) The method of claim 46, wherein said activity is a phosphorylation activity and/or an autophosphorylation activity.

48. (Original) The method of claim 46, wherein said contacting is effected *in vitro*.

49. (Original) The method of claim 46, wherein said contacting is effected *in vivo*.

50-62. (Canceled)

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

63. (Original) The method of claim 46, further comprising contacting said cells with at least one an additional active ingredient, said additional active ingredient being capable of altering an activity of GSK-3.

64. (Original) The method of claim 63, wherein said additional active ingredient is insulin.

65. (Original) The method of claim 63, wherein said additional active ingredient is capable of inhibiting an activity of GSK-3.

66. (Canceled)

67. (Original) The method of claim 63, wherein said additional active ingredient is capable of downregulating an expression of GSK-3.

68-70. (Canceled)

71. (Currently Amended) A method of potentiating insulin signaling, the method comprising contacting insulin responsive cells with an effective amount of a~~the~~ conjugate comprising:

(a) a polypeptide having the amino acid sequence :

$$[Yn\cdots Y_1]ZX_1X_2X_3S(p)[W_1\cdots Wm]$$

wherein,

m equals 1 or 2;

n is an integer from 1 to 50;

S(p) is a phosphorylated serine residue or a phosphorylated threonine residue;

Z is any amino acid residue excepting serine residue or threonine residue; and

X_1, X_2, X_3, Y_1-Yn and W_1-Wm are each independently any amino acid residue; and

(b) at least one hydrophobic moiety being attached to said polypeptide,

the conjugate being capable of inhibiting an activity of glycogen synthase kinase-3 (GSK-3), wherein the hydrophobic moiety provides the conjugate with better (i) membrane permeability and/or (ii) interaction with the hydrophobic patch of the GSK-3 ~~of claim 1~~.

72. (Original) The method of claim 71, further comprising contacting said cells with insulin.

73. (Original) The method of claim 71, wherein said contacting is effected *in vitro*.

74. (Original) The method of claim 71, wherein said contacting is effected *in vivo*.

75-87. (Canceled)

88. (Currently Amended) A method of treating a biological condition associated with GSK-3 activity, the method comprising administering to a subject in need thereof a therapeutically effective amount of a~~the~~ conjugate comprising:

(a) a polypeptide having the amino acid sequence :

$[Yn\cdots Y_1]ZX_1X_2X_3S(p)[W_1\cdots Wm]$

wherein,

m equals 1 or 2;

n is an integer from 1 to 50;

S(p) is a phosphorylated serine residue or a phosphorylated threonine residue;

Z is any amino acid residue excepting serine residue or threonine residue; and

X_1, X_2, X_3, Y_1-Yn and W_1-Wm are each independently any amino acid residue; and

(b) at least one hydrophobic moiety being attached to said polypeptide,

the conjugate being capable of inhibiting an activity of glycogen synthase kinase-3 (GSK-3), wherein the hydrophobic moiety provides the conjugate with better (i) membrane permeability and/or (ii) interaction with the hydrophobic patch of the GSK-3 ~~of claim 1~~.

89. (Previously Presented) The method of claim 88, wherein said biological condition is selected from the group consisting of obesity, non-insulin dependent diabetes mellitus, an insulin-dependent condition, an affective disorder, a neurodegenerative disease or disorder and a psychotic disease or disorder.

90. (Withdrawn) The method of claim 89, wherein said affective disorder is selected from the group consisting of a unipolar disorder and a bipolar disorder.

91-92. (Canceled)

93. (Withdrawn) The method of claim 89, wherein said neurodegenerative disorder results from an event selected from the group consisting of cerebral ischemia, stroke, traumatic brain injury and bacterial infection.

94. (Withdrawn) The method of claim 89, wherein said neurodegenerative disorder is a chronic neurodegenerative disorder.

95. (Withdrawn) The method of claim 94, wherein said chronic neurodegenerative disorder results from a disease selected from the group consisting of Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS associated dementia, amyotrophic lateral sclerosis (AML) and multiple sclerosis.

96. (Withdrawn) The method of claim 89, wherein said psychotic disorder is schizophrenia.

97. (Previously Presented) The method of claim 88, further comprising administering to the subject at least one additional active ingredient, said at least one additional active ingredient being capable of altering an activity of GSK-3.

98. (Previously Presented) The method of claim 97, wherein said additional active ingredient is insulin.

99. (Previously Presented) The method of claim 97, wherein said additional active ingredient is capable of inhibiting an activity of GSK-3.

100. (Canceled)

101. (Previously Presented) The method of claim 97, wherein said additional active ingredient is capable of downregulating an expression of GSK-3.

102-117. (Canceled)

118. (Withdrawn) A method of treating an affective disorder, the method comprising administering to a subject in need thereof a therapeutically effective amount of at least one compound that is capable of specifically inhibiting an activity of GSK-3.

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

119. (Withdrawn) The method of claim 118, wherein said affective disorder is selected from the group consisting of a unipolar disorder and bipolar disorder.

120. (Withdrawn) The method of claim 119, wherein said unipolar disorder is depression.

121. (Withdrawn) The method of claim 119, wherein said bipolar disorder is manic depression.

122. (Withdrawn) The method of claim 118, wherein said compound is a polypeptide having the amino acid sequence:

$$[Yn\cdots Y_1]ZX_1X_2X_3S(p)[W_1\cdots Wm]$$

wherein,

m equals 1 or 2;

n is an integer from 1 to 50;

S(p) is a phosphorylated serine residue or a phosphorylated threonine residue;

Z is any amino acid residue excepting serine residue or threonine residue; and

X_1, X_2, X_3, Y_1-Yn and W_1-Wm are each independently any amino acid residue.

123. (Withdrawn) The method of claim 122, wherein Y_3 is any amino acid residue except a glutamic acid residue.

124. (Withdrawn) The method of claim 122, wherein Z is an alanine residue.

125. (Withdrawn) The method of claim 122, wherein n is an integer from 1 to 15.

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

126. (Canceled)

127. (Withdrawn) The method of claim 122, wherein said polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequences set forth in SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:12.

128. (Withdrawn) The method of claim 122, wherein said polypeptide further comprises at least one hydrophobic moiety being attached thereto.

129. (Withdrawn) The use of claim 128, wherein said at least one hydrophobic moiety is attached to an N-terminus and/or a C-terminus of said polypeptide.

130. (Canceled)

131. (Withdrawn) The method of claim 128, wherein said at least one hydrophobic moiety comprises a hydrophobic peptide sequence.

132. (Withdrawn) The method of claim 131, wherein said hydrophobic peptide sequence comprises at least five consecutive amino acid residues selected from the group consisting of an alanine residue, a cysteine residue, a glycine residue, an isoleucine residue, a leucine residue, a valine residue, a phenylalanine residue, a tyrosine residue, a methionine residue, a proline residue and a tryptophan residue.

133. (Withdrawn) The method of claim 128, wherein said at least one hydrophobic moiety comprises a fatty acid.

134. (Withdrawn) The method of claim 133, wherein said fatty acid is attached to at least one amino acid residue.

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

135. (Withdrawn) The method of claim 133, wherein said fatty acid is selected from the group consisting of myristic acid, lauric acid, palmitic acid, stearic acid, oleic acid, linoleic acid and linolenic acid.

136-140. (Canceled)

141. (Withdrawn) The method of claim 128, wherein said compound has the amino acid sequence set forth in SEQ ID NO:16.

142. (Withdrawn) A method of up-regulating a β-catenin level in a hippocampus of a subject in need thereof, the method comprising administering to the subject a thera[eutically effective amount of at least one compound that is capable of specifically inhibiting an activity of GSK-3.

143. (Withdrawn) The method of claim 142, wherein said compound is a polypeptide having the amino acid sequence:

$$[Yn\cdots Y_1]ZX_1X_2X_3S(p)[W_1\cdots Wm]$$

wherein,

m equals 1 or 2;

n is an integer from 1 to 50;

S(p) is a phosphorylated serine residue or a phosphorylated threonine residue;

Z is any amino acid residue excepting serine residue or threonine residue; and

X_1, X_2, X_3, Y_1-Yn and W_1-Wm are each independently any amino acid residue.

144. (Withdrawn) The method of claim 143, wherein Y_3 is any amino acid residue except a glutamic acid residue.

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

145. (Withdrawn) The method of claim 143, wherein Z is an alanine residue.

146. (Withdrawn) The method of claim 143, wherein n is an integer from 1 to 15.

147. (Canceled)

148. (Withdrawn) The method of claim 143, wherein said polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequences set forth in SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:12.

149. (Withdrawn) The method of claim 143, wherein said polypeptide further comprises at least one hydrophobic moiety being attached thereto.

150. (Withdrawn) The use of claim 149, wherein said at least one hydrophobic moiety is attached to an N-terminus and/or a C-terminus of said polypeptide.

151. (Canceled)

152. (Withdrawn) The method of claim 149, wherein said at least one hydrophobic moiety comprises a hydrophobic peptide sequence.

153. (Withdrawn) The method of claim 152, wherein said hydrophobic peptide sequence comprises at least five consecutive amino acid residues selected from the group consisting of an alanine residue, a cysteine residue, a glycine residue, an isoleucine residue, a leucine residue, a valine residue, a phenylalanine residue, a tyrosine residue, a methionine residue, a proline residue and a tryptophan residue.

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

154. (Withdrawn) The method of claim 149, wherein said at least one hydrophobic moiety comprises a fatty acid.

155. (Withdrawn) The method of claim 154, wherein said fatty acid is attached to at least one amino acid residue.

156. (Withdrawn) The method of claim 154, wherein said fatty acid is selected from the group consisting of myristic acid, lauric acid, palmitic acid, stearic acid, oleic acid, linoleic acid and linolenic acid.

157-161. (Canceled)

162. (Withdrawn) The method of claim 149, wherein said compound has the amino acid sequence set forth in SEQ ID NO:16.

163. (Original) A process of producing the conjugate of claim 1, the process comprising:

providing said polypeptide;

providing said at least one hydrophobic moiety; and

conjugating said at least one hydrophobic moiety and said polypeptide.

164-178. (Canceled)

179. (New) A conjugate comprising:

(a) a polypeptide having the amino acid sequence:

$$[Yn\cdots Y_1]ZX_1X_2X_3S(p)[W_1\cdots Wm]$$

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

wherein,

m equals 1 or 2;

n is an integer from 3 to 7, such that said polypeptide consists of 10 to 13 amino acid residues;

S(p) is a phosphorylated serine residue or a phosphorylated threonine residue;

Z is any amino acid residue excepting serine residue or threonine residue; and

X_1, X_2, X_3, Y_1-Yn and W_1-Wm are each independently any amino acid residue; and

(b) at least one hydrophobic moiety being attached to said polypeptide, said at least one hydrophobic moiety being a hydrophobic peptide sequence which consists of at least five consecutive amino acid residues selected from the group consisting of an alanine residue, a cysteine residue, a glycine residue, an isoleucine residue, a leucine residue, a valine residue, a phenylalanine residue, a tyrosine residue, a methionine residue, a proline residue and a tryptophan residue,

the conjugate being capable of inhibiting an activity of glycogen synthase kinase-3 (GSK-3), wherein the hydrophobic moiety provides the conjugate with better (i) membrane permeability and/or (ii) interaction with the hydrophobic patch of the GSK-3.

180. (New) The conjugate of claim 179, wherein said at least one hydrophobic moiety is attached to an N-terminus and/or a C-terminus of said polypeptide.

181. (New) The conjugate of claim 179, wherein Y_3 is any amino acid residue except a glutamic acid residue.

182. (New) The conjugate of claim 179, wherein Z is an alanine residue.

183. (New) A pharmaceutical composition comprising, as an active ingredient, the conjugate of claim 179, and a pharmaceutically acceptable carrier.

In re Application of: ELDAR-FINKELMAN
Serial No.: 10/538,171
Filed: December 8, 2005
Office Action Mailing Date: August 20, 2007

Examiner: Russel, Jeffrey E.
Group Art Unit: 1654
Attorney Docket: 29724

184. (New) The pharmaceutical composition of claim 183, packaged in a packaging material and identified in print, on or in said packaging material, for use in the treatment of a biological condition associated with GSK-3 activity.

185. (New) The pharmaceutical composition of claim 184, wherein said biological condition is selected from the group consisting of obesity, non-insulin dependent diabetes mellitus, an insulin-dependent condition, an affective disorder, a neurodegenerative disease or disorder and a psychotic disease or disorder.

186. (New) The pharmaceutical composition of claim 183, further comprising at least one additional active ingredient that is capable of altering an activity of GSK-3.